

IN THE CLAIMS

The listing of the claims which follows replaces any and all prior versions and/or listings of the claims in the application.

1. (Original) A mutated peroxisome proliferator-activated receptor (PPAR) ligand binding domain polypeptide comprising the amino acid sequence of a mutated PPAR ligand binding domain, wherein said mutated PPAR ligand binding domain is

- (a) bound by a partial PPAR agonist; and
- (b) bound or activated by a full PPAR agonist to a lesser extent than the wild-type receptor.

2. (Original) The mutated PPAR ligand binding domain polypeptide of claim 1, wherein said mutated PPAR ligand binding domain selectively binds said partial agonist.

3. (Original) The mutated PPAR ligand binding domain polypeptide of claim 1, wherein said mutated PPAR ligand binding domain polypeptide is selectively activated by said partial agonist.

4. (Original) The mutated PPAR ligand binding domain polypeptide of claim 1, wherein said mutated ligand bind domain is either:

a mutated human PPAR α ligand binding domain, wherein a residue corresponding to tyrosine 464 is selected from the group consisting of: alanine, valine, leucine, isoleucine, proline, tryptophan, phenylalanine, methionine, histidine, asparagine, and glutamine;

a mutated human PPAR δ ligand binding domain, wherein a residue corresponding to tyrosine 437 is selected from the group consisting of: alanine, valine, leucine, isoleucine, proline, tryptophan, phenylalanine, methionine, histidine, asparagine, and glutamine, or

a mutated human PPAR γ ligand binding domain, wherein a residue corresponding to tyrosine 473 is selected from the group consisting of: alanine, valine, leucine, isoleucine, proline, tryptophan, phenylalanine, methionine, histidine, asparagine, and glutamine.

5. (Original) The mutated PPAR ligand binding domain polypeptide of claim 1, where said polypeptide comprises the amino acid sequence of SEQ ID NO: 4:
QLNPESADLRALAKHLYDSYIKSFPLTKAKARAILTGKTTDKSPFVIYDMNSLMM
GEDKIKFKHITPLQEQSKEVAIRIFQGCQFRSVEAVQEITEYAKSIPGFVNLDLNDQ
VTLLKYGVHEIITYTMLASLMNKDGVLISEGQGFMTREFLKSRLKPFQDFMEPKFE
FAVKFNALELDDSDLAIFIAVILSGDRPGLLNVPKPIEDIQDNLLQALELQLKLNHP
ESSQLFAKLLQKMTDLRQIVTEHVQLLQVIKKTETDMSLHPLLQEIXKDLY
wherein X is selected from the group consisting of: alanine, valine, leucine, isoleucine, proline, tryptophan, phenylalanine, methionine, histidine, asparagine, and glutamine.

6. (Original) The mutated PPAR ligand binding domain polypeptide of claim 5, wherein X is phenylalanine or alanine.

7. (Original) A ligand-activated transcription factor comprising the mutated PPAR ligand binding domain of claim 1 and a DNA binding domain.

8. (Original) The ligand-activated transcription factor of claim 7, wherein said transcription factor can be selectively activated by partial agonist binding.

9. (Original) The ligand-activated transcription factor of claim 8, wherein said mutated ligand bind domain is either:

a mutated human PPAR α ligand binding domain, wherein a residue corresponding to tyrosine 464 is selected from the group consisting of: alanine, valine,

leucine, isoleucine, proline, tryptophan, phenylalanine, methionine, histidine, asparagine, and glutamine;

a mutated human PPAR δ ligand binding domain, wherein a residue corresponding to tyrosine 437 is selected from the group consisting of: alanine, valine, leucine, isoleucine, proline, tryptophan, phenylalanine, methionine, histidine, asparagine, and glutamine, or

a mutated human PPAR γ ligand binding domain, wherein a residue corresponding to tyrosine 473 is selected from the group consisting of: alanine, valine, leucine, isoleucine, proline, tryptophan, phenylalanine, methionine, histidine, asparagine, and glutamine.

10. (Original) The ligand-activated transcription factor of claim 7, where said mutated ligand binding domain consists of the amino acid sequence of SEQ ID NO: 4:

QLNPESADLRALAKHLYDSYIKSFPLTKAKARAILTGKTTDKSPFVIYDMNSLMM
GEDKIKFKHITPLQEQSKEVAIRIFQGCQFRSVEAVQEITEYAKSIPGFVNLDLNDQ
VTLLKYGVHEIITYTMLASLMNKDGVLISEGQGFMTREFLKSRLKPFMGDFMEPKFE
FAVKFNALELDDSDLAIFIAVIILSGDRPGLLNVPKPIEDIQDNLLQALELQLKLNHP
ESSQLFAKLLQKMTDLRQIVTEHVQLLQVIKKTETDMSLHPLLQEIXKDLY

wherein X is selected from the group consisting of: alanine, valine, leucine, isoleucine, proline, tryptophan, phenylalanine, methionine, histidine, asparagine, and glutamine.

11. (Original) The ligand-activated transcription factor of claim 10, wherein X is phenylalanine or alanine.

12. (Original) The ligand-activated transcription factor of claim 11, wherein said transcription factor is a chimeric receptor.

13. (Original) The ligand-activated transcription factor of claim 12, wherein said transcription factor consists of the amino acid sequence of SEQ ID NO: 5 or SEQ ID NO: 6.

14. (Original) A method of making a mutated PPAR ligand binding domain polypeptide comprising the step of mutating a PPAR ligand binding domain such that an amino acid present in a wild-type PPAR ligand binding domain that makes a direct interaction with a full agonist either makes no interaction, or a substantially different interaction, with said full agonist.

15. (Original) The method of claim 14, wherein said mutating produces said mutated PPAR ligand binding domain polypeptide such that said mutated PPAR ligand binding is selectively bound or activated by a partial PPAR agonist.

16. (Original) The method of claim 15, wherein said mutating comprises changing an amino acid that makes a direct interaction with a full agonist into an amino acid that either makes no interaction, or a substantially different interaction, with said full agonist.

17. (Original) The method of claim 16, wherein said PPAR ligand binding domain that is mutated comprises SEQ ID NO: 3:

QLNPESADLRALAKHLYDSYIKSFPLTKAKARAILTGKTTDKSPFVIYDMNSLMM
GEDKIKFKHITPLQEQSKEVAIRIFQGCQFRSVEAVQEITEYAKSIPGFVNLDLNDQ
VTLLKYGVHEIYTMLASLMNKDGVLISEGQGFMTREFLKSRLKPFQDFMEPKFE
FAVKFNALELDDSDLAIFIAVIILSGDRPGLLNVPKPIEDIQDNLLQALELQLKLNHP
ESSQLFAKLLQKMTDLRQIVTEHVQLLQVIKKTETDMSLHPLLQEIYKDLY.

18. (Currently Amended) A nucleic acid comprising a nucleotide sequence encoding the polypeptide of ~~any one of claims 1-6 or the transcription factor of any one claims 7-13~~ claim 1.

19 - 21 (Canceled)

22. (Currently Amended) A method of assaying for a partial PPAR agonist comprising the step of measuring the ability of a test compound to bind to or activate the polypeptide of ~~any one of claims 1-6 or the transcription factor of any one of claims 7-13~~ claim 1.

23. (New) A nucleic acid comprising a nucleotide sequence encoding the transcription factor ~~polypeptide~~ of claim 7.